FORMULATION SCIENCE

VOLUME I

Proceedings from Formulations Forum '97

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Published by
The Association of Formulation Chemists

Making Useful Products Usable

RECENT TRENDS IN PESTICIDE FORMULATIONS

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CONTENTS

ABSTRACT

This paper describes the objectives of pesticide formulations and the impact of newly emerging requirements of the pesticide industry. The importance of research work based on pesticide delivery system is pointed out. The problems of conventional formulations are discussed as well as

methods for their improvement giving rise to new formulations types. New and promising formulations such as water-based formulations, water dispersible granules, water soluble packages, controlled release formulations such as microcapsules and polymeric pesticides, biopesticide formulations and other functional formulations are reviewed; their advantages and future trends are also discussed.

I. INTRODUCTION

A. PURPOSES OF PESTICIDE FORMULATIONS

Pesticides are usually effective at several grams to hundreds of a grams of active ingredient per 10 ares (1000^2 meters). However, it is very difficult to apply such a small amount uniformly to a broad field. Therefore, pesticide technical materials are diluted with suitable solid or liquid diluents in order to spray or apply easily. This is "Pesticide Formulation". In this case, biological efficacy, storage stability, safety, easy handling, and cost should be taken into consideration to commercialize pesticide formulations.

The purposes of such pesticide formulations are summarized as follows:

- To make handling and application of the pesticides easy.
- To maximize biological efficacy.
- To improve defects in the pesticide.
- To make pesticides safer for workers and users.
- To reduce harmful effects and impact on the nontarget organisms and the environment.
- To improve work efficiency that results in labor savings.
- To give various functions to pesticides in order to broaden their spectrum of activity.

B. RECENT REQUIREMENTS OF PESTICIDE INDUSTRY

A recent trend is the more stringent regulatory requirements on the pesticide industry, especially with regard to toxicity. Pesticides are being required to satisfy the following conditions.[81]

- Higher safety: A pesticide should be safe for workers and have no harmful effect or impact on nontarget organisms or the environment.
- High efficacy: Pesticides should have good initial and residual efficacy at lower dosage.
- Lowest possible price: Manufacturing cost should be low and cost performance should be good.
- Less labor intensive: The application should be easy and application efficiency should be high.

It is not easy for candidate compounds by themselves to satisfy all these requirements. It has thus become very difficult to develop new pesticides; the cost and time for the development of a new pesticide has increased

significantly. Therefore, it becomes very important to improve formulation and application technology in order to satisfy the above requirements for new and existing active ingredients. To this end, formulation research has become very important; meeting the last four items in the above list has become essential.

II. PESTICIDE DELIVERY SYSTEM

In order to meet recent requirements of pesticide industry, the concept of "Pesticide Delivery System"(PDS) is very important.[30,78,81] PDS can be defined as a technique or a method in which active ingredients are made available to a specified target at a concentration and duration designed to accomplish an intended effect, i.e., obtain the fullest biological efficacy while minimizing various harmful effects. The concept of PDS is very similar to that of Drug Delivery System (DDS). However, as compared to DDS, PDS has the following difficulties that have to be addressed.

- PDS is an open system, while DDS is a closed system.
- PDS has variable conditions of natural circumstances, while• DDS has constant conditions such as temperature.
- PDS has no natural delivery vehicle to the targets such as insects, fungi and weeds, while in the case of DDS the blood delivers the drug to the target organs.
- In the case of PDS, cheaper materials and technologies can be used – as pesticide users are much more cost-conscious than consumers of pharmaceutical drugs.

Therefore, PDS are not as easily formulated as are DDS. However, research work about formulation and application technologies based on this concept should be continuously carried out.

III. IMPROVEMENT OF FORMULATIONS AND APPLICATION TECHNOLOGIES.

Various improvements of formulations and application technologies have been made according to the recent demand of the pesticide industry. Changes in formulation types have also proceeded and various new types of formulations and application methods have been developed.

Table 1 shows some of the problems of conventional formulations, the reasons behind these problems, and methods for reducing them in new pesticide formulations being developed.[76,78,79]

Emulsifiable concentrates (EC) have problems of toxicity, phytotoxicity and flammability that are caused by organic solvents and synthetic surface-active agents used in EC.

One of the improvement methods is making use of water, the safest liquid, instead of organic solvents in emulsions and microemulsions. The

other method is solidifying of EC formulations, which results in emulsifiable granules or powders). Another method is making use of safer organic solvents and emulsifiers.

Table 1
Development of New Pesticide Formulations

Formulation	Problems	Reasons	Improvement methods	New formulations
Emulsifiable Concentrate	Toxicity; phytotoxicity; flammable	Organic solvent, suface active agents	Use water; solidify; change solvents or emulsifiers	Concentrated emulsions (EW, CE) Microemulsions (ME) Suspoemulsions (SE) Emulsifiable granule or powder
Wettable Powder	Dusty	Fine powder	Water dispersion, granulate, package in water soluble bags	Suspension concentrate (SC, Flowable) Water dispersible granule (WDG) Water soluble packages
Dust	Drift; dusty	Fine powder	Granulate: remove fine particles	DL dust Fine granule F
Flowable	Deterioration of physical properties	Dispersion in liquid	Remove liquid Improve recipe	Dry flowable Improved formulation
Granule	Weight	3-kg/10 are	Higher concentration	1 Kg granules

Wettable powders (WP) have a problem of dustiness, both at the time of dilution and after drying of the sprayed liquid, that is caused by fine mineral powder used in the WP as diluents. One of the improvement methods is dispersing WP's in water to make a flowable formulations. The other method is granulating WP to result in water dispersible granules (WG). Another method is packaging the WP in water-soluble packages.

Dust has a problem of drift, which is caused by fine mineral powder used as carriers. One method of improvement is by removing particles less than 10 microns resulting in a DL dust (driftless dust having an average particle size >20 microns). Another method of improvement is granulating the formulation into fine granules (F) having a particle size of 63-212 microns. Both the DL dust and the fine granule F have been developed in Japan.

Flowable formulations have a problem of deterioration of physical properties, that is, sedimentation. One improvement method is to remove the liquid resulting in dry flowable, water-dispersible powders.

Granule formulations have a problem of weight, considering application rates of 3-kg per 10-ares that is common in Japan. The method of improvement is to increase the active ingredient concentration in the formulation. A new, higher dose 1-kg granule formulation which will treat 10-ares, has been introduced in Japan.

Table 2 shows general recent requirements in the pesticide industry, methods of improvement, and new types of formulations.

Controlled release formulations such as microcapsules are developed for improved safety, labor saving, and improved biological efficacy.

For labor saving, there have been developed application methods of pesticides from levees and water inlets of paddy fields, application at the same time of transplantation, application to the nursery box, seed treatments and application of pesticides with fertilizers. Corresponding to these application methods, various new types of formulations have been developed such as jumbo herbicides, water surface spreading formulations, and fertilizers containing pesticides.

Biopesticides are also developed for improved safety and improved biological efficacy.

From these arguments, it is clear that improvements can be summarized as follows:

- Using water instead of organic solvents resulting in water-based formulations.
- Granulation or water-soluble packaging of dusty formulations.
- Development of controlled release formulations such as microcapsules, laminates, granules, and polymeric pesticides.
- Development of various functional formulations such as jumbo formulations, water surface spreading formulations, and fertilizers containing pesticides.
- Using various kinds of biopesticides.

Table 2
Recent Requirements in the Pesticide Industry, Methods of Improvement, and New Types of Formulations

Recent Requirements	Methods of Improvement	New Types of Formulations
	Controlled release	**Controlled Release Formulation**
Improved safety Labor-saving Improved biological efficacy	Exposure reduction; Application from levee; Application from water inlet of paddy field; Application of pesticides to nursery box; Application of pesticides at the same time of transplantation; Seed treatment	(microcapsule, laminate, granule) Water soluble package Jumbo herbicide
	Application of pesticides with fertilizers Making use of biopesticide Targeting	Fertilizer containing pesticide Biopesticide formulation Surface spreading formulation

IV. NEW AND PROMISING FORMULATIONS

A. WATER-BASED FORMULATIONS[76-78]

Water-based formulations are obtained by emulsifying or suspending pesticide technical materials in water. Water is the safest liquid. Therefore, water-based formulations have various advantages from a safety point of view. On the other hand, they have also some kinds of disadvantages. For example, pesticides that are unstable in water can not generally be formulated into water-based formulations. However, various kinds of technologies have been developed to stabilize the pesticides that are unstable in water. Each water-based formulation will be discussed in more detail.

1. Emulsion, Oil in Water (EW)[21,30,45,58,62]

This formulation is obtained by emulsifying or dispersing water-insoluble pesticides in the liquid state in water by means of proper emulsifiers. The pesticides, which are liquid at room temperature, can be dispersed as they are in water. Solid pesticides are dissolved at first in water-insoluble organic solvents, and then dispersed in water. In this case, it is better that water solubility is lower than 1000 ppm. This formulation includes active ingredients, emulsifiers, thickening agents, antifreeze, preservatives, defoamers, (organic solvents), and water. As emulsifiers, synthetic emulsifiers are commonly used such as the mixture (HLB >14) of polyoxyethylene (40 mole) castor oil ether and polyoxyalkyleneglycol ether, and water soluble polymers such as polyvinyl alcohol and gum arabic, which act as protective colloids are also used. As thickening agents, acrylic polymers, cellulose derivatives, and xanthan gum are frequently used, as these materials show thixotropic properties. Fine mineral powders such as bentonite, hydrated silicon dioxide are also applied.

The advantages of this formulation are as follows:

- Reduced toxicity and irritation.
- No dust problems.
- Nonflammable.
- Better efficacy than WP due to smaller particle size.
- Reduced phytotoxicity.
- Nonstaining.
- Reduced smell.
- Plastic bottles can be used.

The disadvantage is that an emulsion is thermodynamically unstable dispersion. Therefore it tends to lose its uniformity after keeping for long time at room temperature through coalescence, coagulation, creaming, or settling to result in phase separation. The emulsion is also very sensitive to temperature. Therefore, stability of the emulsion may be lost by change of temperature. Dissolving them in organic solvents can often stabilize

emulsions of pesticides that are unstable in water.

2. **Suspension Concentrate (SC, flowable)**[11,30,55,62,69]

This formulation is obtained by suspending solid water-insoluble pesticides in water. The purpose of this formulation is to formulate pesticides insoluble in both water and organic solvents, into flowable liquid formulation. These formulations contain active ingredients, dispersing agents, wetting agents, thickener, anti-freeze, preservatives, defoamer, specific gravity adjuster and water. Pesticide technical materials should satisfy the following conditions.

- Melting point is higher than 60°C.
- Water solubility is less than 100 ppm.
- They should not be easily hydrolyzed.
- They can be milled to small particles and Ostwald ripening does not take place.

Dispersing agents act as dispersion stabilizers. There are two stabilization mechanisms, static electric repulsion force and steric stabilization.[11,18,27,61] In order to stabilize by static electric repulsion force, anionic Surfactants such as polyoxyethylene phosphate and polyoxyethylene sulfates are widely used. These surfactants adsorb to the dispersed particles to give a negative electric charge, which stabilizes the dispersion by the repulsion force between negative charges. Polymers and high molecular weight nonionic surfactants form thicker adsorbed layers on the dispersed particles. For steric stabilization, water-soluble polymers such as lignosulphonate, polyvinylalcohol and alkylnaphthalene formalin condensates are often used. As wetting agents, which make pesticide technical materials wet in water, polyoxyethylene alkylphenylether and polyoxyethylene sorbitan ester are often used. Dispersing agents may act also as wetting agents. As thickeners, the same materials as described in "emulsion" can be used. Colloidal microcrystalline cellulose is also used for a thickener.[29] Inorganic electrolytes such as sodium chloride and calcium chloride act as specific gravity adjusters to reduce differences between specific gravities of liquid layers and dispersed particles. It is also reported that polyethyleneglycol enhances the stability of concentrated suspension.[40]

The advantages of this formulation are the same as those of "Emulsion".

The disadvantages are as follows:

- Hydrolyzable pesticide technical materials can not be formulated to this formulation.
- Sometimes a hard cake is formed.
- High concentration formulation is impossible.
- Wet grinding process is expensive.

Stable suspension formulations of hydrolytically unstable sulfonylurea compounds were developed by the regulation of suspension pH and

complexation.[28]

This formulation is usually sprayed after dilution with water. Recently there have been developed flowable herbicides which have good diffusion properties in water and can be applied without dilution by hands from levees of paddy fields[70-72] smaller than 0.3 ha. In this case, proper surfactants are chosen for active ingredients to diffuse and spread smoothly in water. The concentration of active ingredients reaches an even level within 1-day in paddy water and within 3-days on the soil surface. This application method of flowable proved to reduce labor intensity in applications by 30% in comparison with conventional granular herbicides.

In order not to stick to rice and to reduce phytotoxicity, surface tension is adjusted to be 36-65 dyne/cm at 25°C by selecting appropriate surfactants.[70,71]

Another application method has been developed where the flowable herbicides are added to the irrigation water inlets.

3. Suspoemulsion (SE)[30,42,62,89]

This formulation is a combination of emulsion and suspension. Both solid and liquid technical materials are dispersed in water. Usually, solid technical materials are formulated into SC and liquid technical materials are formulated into EW; when they are sprayed at the same time, they should be tank-mixed before application. It is a great advantage of suspoemulsions that water-insoluble solids and liquid technical materials can both be dispersed/emulsified with water being the continuous phase. The advantages of this formulation are the same as those of EW and SC. By using suspoemulsions, not only are the number of applications reduced resulting in savings in time and money, but formulation costs can also be reduced. This formulation is very promising because of its safety and application advantages, but few such formulations have been developed due to the difficulty to develop stable formulations, as mentioned below.

In suspoemulsions, generally two kinds of surfactants are necessary, emulsifier to emulsify oily liquid technical materials and dispersant to disperse solid technical materials. They should be compatible in one formulation. A proper surface active agent may act as both an emulsifier and a dispersant. When adsorption characteristics to solid and emulsion particles are different, stable emulsion or dispersion can not be obtained. Therefore, selection of appropriate surfactants is significantly important but considerably difficult. At present, they are selected by the method of trial and error for each formulation. However, an easy method for the preparation of a suspoemulsion using latexes as emulsion stabilizers was also been reported.[43] Alkylglucoside surfactants have been successfully utilized in both phases of a suspoemulsion.[15]

Microemulsion (ME) [30,45]

Microemulsion is a transparent or semitransparent, one liquid phase, and thermodynamically stable emulsion system. Particle sizes of microemulsions are about 0.01-0.1 microns. Therefore, neither creaming nor settling takes place during storage. This formulation has advantages similar to emulsions, but the following additional advantages are realized:

- Emulsion is quite stable for a long time.
- Emulsion particle size is smaller than that of EC, and biological efficacy may be superior.
- It has a clean image and the value of commercial goods is high.

There are, however, some drawbacks as follows:

- High concentration formulation can not be made.
- It is transparent even after dilution. Therefore, it is difficult to know whether it is diluted or not.

This formulation contains active ingredients, emulsifiers, cosurfactants, and water. When active ingredients are solid, water immiscible organic solvents such as aromatic hydrocarbons are used to dissolve them. The amount of emulsifiers is larger than that in emulsion. For example, about 20% emulsifiers are necessary in order to make microemulsion containing 10% of active ingredients. Combinations of strong hydrophilic (HLB >13) and high molecular weight nonionic surfactants and hydrophobic anionic surfactants are the preferred emulsifiers. For example, polyoxyethylene (15-30 mole), styrylphenol ether, polyoxyethylene phenylphenol ether, and calcium dodecylbenzene sulphonate are used for microemulsions of pyrethroid and organophosphorus insecticides.[30,87] Tristyrylphenol-based surfactants are also used for microemulsion of pyrethroids.[10] Stable microemulsion was obtained by using mixed surfactants, one being a higher N-alkylpyrrolidone, which functioned as interfacial solvents.[46] As cosurfactants, nonionic surfactant with low HLB or C_4 to C_{10} alcohols[57] are used in order to lower the HLB of the formulation and to reduce surface tension between water and oil. As solvents, fatty acid methyl ester containing carbon chain length of 8-12 provide maximum solubility and emulsification characteristics.[64]

Multiple Emulsion [1]

This formulation is an emulsion of an emulsion. In the w/o/w multiple emulsion, active ingredients within the inner water phase can not diffuse freely into the external continuous water phase. Therefore, it is possible to put incompatible active ingredients in other compartments within a single formulation. The multiple emulsions reduce toxicity significantly. This formulation type is just starting to be applied to pesticide formulations, and improvement of formulation stability is essential.

B. WATER DISPERSIBLE GRANULE (WG, DRY FLOWABLE)[12,23,30,62,76-79,85]

Water dispersible granules were developed to prevent dustiness of wettable powders at the time of dilution, and this formulation disintegrates and disperses readily in water after application.

The advantages of this formulation are as follows:

- Dust free and safe for workers.
- High density and compact packaging.
- Constant apparent density and measurable by volume.
- Good flowability and superior handling.
- Possibility of high concentration formulation.
- Packageable in paper bags and various containers.
- Little residue in the container and the used containers are easily disposed of.

Water dispersible granule can be formulated by various methods. Characteristics of each method and physicochemical properties of WG formulated by each method are summarized in Table 3. It is clear that the physicochemical properties of WG depend on formulation methods. Formulation recipes should be varied according to the formulation methods.

Water dispersible granules generally contain active ingredients, wetting agents, dispersants, fillers, binders, disintegrants, antifoams, and adjuvants. The kind of dispersants in the formulation is the most important.

The development of water dispersible granules of liquid and low melting technical materials was initially difficult, but recent advances in technology have simplified this problem. In this case, the most important factor in the formulation is the carrier. It was found that the low melting technical requires precipitated silica and that the liquid technical requires calcium silicate.[44]

Commercial water dispersible granules are formulated mainly by either a spray drying method, pan granulation method, high speed mixing method, or extrusion method. Recently, the extrusion method has become more popular.

C. WATER-SOLUBLE PACKAGES[20,24,68]

Water-soluble packaging of pesticides has various advantages as follows:

- Reduction of worker exposure at the time of dilution of a WP.
- Safe and easy handling.
- Unit dose convenience.
- Uncontaminated packaging waste.

Water-soluble packaging has been carried out for about 20 yr, mainly because of the first two advantages mentioned above. This has become very important from the viewpoint of package disposal. When water-soluble bags are used for pesticides, the outer layer has to protect the inner bag from

moisture and also be uncontaminated with the pesticide. This is a big advantage for disposal of the packaging materials.

Polyvinylalcohol (PVA) is the most used water-soluble film. The physicochemical properties of PVA have been improved significantly, including water solubility, physical strength, processability, and stability. More products are being packaged in water-soluble bags due to the above mentioned advantages. Initially solid formulations were packaged in water-soluble bags, and later liquid formulations such as EC were also packaged in water-soluble bags. In this case leaking through pinholes took place. Therefore recently, high viscous gel formulations are packaged in water-soluble bags instead of EC.

In Japan, herbicide granules packaged by water-soluble film have been developed for labor - saving application. This formulation is one kind of jumbo herbicides as described later.[32,48] This packaged formulation, which is discussed in more detail below, is thrown by hand from levees into a paddy field. Recently the similar application method of granules packaged by water-soluble film has been developed for insecticides and fungicides. In these cases, most of the granules are spread on water surface to get better biological efficacy.

Water-soluble bottles (50 ml) made of PVA are also used for an oil formulation for rice pest control which spreads over the entire water surface of the paddy field in a few minutes. Six to ten bottles are thrown by hand from the levees into 10-are paddy field.

Table 3
Granulation Methods of WG and Their Characteristics

Granulation Method	Manufacturing conditions: Milling	Moisture Content to be dried (%)	Drying temperature (°C)	Physicochemical properties of WG: Shape	Particle size (mm)	Disintegrability in water	Manufacturing Cost
Spray drying	Wet	40-50	>100	Spherical	0.1-0.5	Excellent	Expensive
Fluidized bed drying	Wet	40-50	50-80	Nearly spherical	0.1-1.0	Excellent	Expensive
Freeze drying	Wet	40-50	<0	Irregular	0.5-3.0	Good	Moderately expensive
Pan granulation	Dry	10-15	50-80	Nearly spherical	0.2-3.0	Good	Cheap
Extrusion	Dry	10-15	50-80	Cylindrical	0.7-1.0	Poor	Cheap
High speed mixing	Dry	10-15	50-80	Irregular	0.1-2.0	Good	Moderately expensive
Fluidized bed	Dry	20-30	50-80	Nearly spherical	0.1-1.0	Good	Moderately expensive
Compression	Dry	0	—	Irregular	0.5-3.0	Poor	Cheap

D. CONTROLLED RELEASE FORMULATIONS

1. Microcapsules (CS)[78,84]

Microcapsules (MC) are small particles (1-1000 microns) composed of a core material and an outer wall. The wall isolates the core material from the environment and protects it from environmental degradation and interaction with other materials. The core materials are designed to be released in a controlled fashion as required. Some review articles are available in the literature.[62,76-86]

Microencapsulation of pesticides is mainly carried out by interfacial polycondensation, *in situ* polymerization and coacervation. Among these methods, interfacial polycondensation is the most useful method for industrial production. Controlling the amount of monomers and process conditions can control particle size and wall thickness relatively easily.

Various polymers used for wall materials of pesticide microcapsules should satisfy the following conditions:

- The polymers have appropriate molecular weight, glass transition temperature, and molecular structure in order to achieve proper release rate.
- The polymers do not react with the pesticides.
- The polymer and its degradation products must not cause any environmental pollution.
- The polymer should be generally stable during storage and usage, and easily manufactured and fabricated into the desired product at acceptable costs.
- For agricultural application, polymers should be biodegradable to avoid environmental pollution.

The general advantages of pesticide microcapsules are as follows:

- Controlled or slow release of core a.i. to result in improvement of residual activity.
- Longer application interval resulting in laborsaving.
- Reduction of application dosage.
- Stabilization of core a.i. against environmental degradation (light, air, humidity, microorganism, etc.).
- Reduction of mammalian toxicity.
- Reduction of human mucous-membrane irritation.
- Reduction of phytotoxicity.
- Reduction of fish toxicity.
- Reduction of evaporation and leaching.
- Reduction of environmental pollution.
- Reduction of reactivity of two insecticides.
- Masking of odor.
- Solidification of liquid pesticides.
- Reduction of drift.

- Increase in the number of target organisms.
- Consistent activity irrespective of application surfaces.
- Easier handling.

An MC does not necessarily have all of the above advantages. Therefore, the proper design of the MC is very important in order to obtain the desired characteristics according to the purpose of the application.

In order to be biologically effective the pesticide must be released from the MC. There are two mechanisms for release.

- Diffusion through the MC wall.
- Destruction of the MC wall by either physical destruction, i.e. mechanical power; or by chemical destruction, i.e. hydrolysis, biodegradation, thermal degradation, etc.

The release behavior described above is controlled by factors such as particle size, wall thickness, type of wall materials, wall structure (porosity, degree of polymerization, crosslink density, additives, etc.), type of core materials (chemical structure, physical state, presence or absence of solvents) and amount or concentration of core materials. Release behavior is determined by interaction of these factors, and optimization is very important for each usage.

In order to get better performance of the MC's for biological efficacy and safer behavior both to workers and environment, time-dependent or site-specific release is desirable. For this purpose, it is essential to develop various functional MC's such as stimuli-responsive MC's that are specific to target organisms. For example, physical pressure-, temperature-, pH-, light-, enzyme- and ion- responsive MC's are desired. These technologies are developing in other application fields.

Examples of commercial pesticide MC's available in Japan are summarized in Table 4. Note that there are more than 60 MC's currently available on the world market. Some of them have been developed very recently. Therefore research and development of microencapsulated pesticides has grown significantly in recent years. This growth has to do with the fact that a lot of advantages mentioned before can meet the current demands of the pesticide industry, that is, safer formulations and application methods which are more labor-saving and environment-friendly. Some examples of functional MC's are explained.

Fenitrothion MC's for cockroach control were developed.[33,53,54,75,80-83,86] The wall material is polyurethane. They were prepared by interfacial polymerization.

These MC's at the rate of 125 mg of a.i./m^2 caused 100% mortality to the German cockroaches even 8-wk after treatment.[33,86] Such a long-lasting residual activity is probably caused by the trampling mechanism, that is, the cockroaches broke the MC's when they contacted the MC's. Breaking of the MC's was confirmed by the microscopic observation of the MC's before and after contact of the cockroaches. Distribution of fenitrothion before and after

cockroaches crawled on the MC-treated petri dish is shown in Fig. 1.[75,86] The amount of fenitrothion outside the MC's was almost negligible before contact. After cockroaches contacted the MC's, however, the amount of fenestration outside the MC's increased significantly. It was also clear that fenitrothion adhering to the body of the cockroaches was 10 times more than that in the viscera.

If trampling is the mode of action, biological efficacy is dependent on the strength of the MC's. It was found that the trampled percentage of MC by the contact of cockroaches can be controlled by D/T as shown in Fig. 2, where D is a mass median diameter and T is a wall thickness.[53,86] D/T is known to be a parameter of MC strength. When the value of D/T is set properly, both initial and residual efficacy were good.

Table 4
Examples of Commercial Pesticide Microcapsules Available in Japan.

Trade name*	Active ingredient	Wall material	Company
Aniverse MC	halfenprox		Mitsui Toatsu Chemical
Baktop	fenobcarb	Polyurethane	Sumitomo Chemical
Diazinon MC	diazinon	polyamide/polyurea	Nippon Kayaku
Diazinon SL Sol	diazinon	polyurea	Nippon Kayaku
Ember MC	permethrin	polyurethane	Sumitomo Chemical
Gokilaht MC	cyphenothrin		Sumitomo Chemical
Guardjet wp (Cell Cap)	*Bacillus thuringiensis* fixed ssp. san diego toxin	*Pseudomonas Fluorescens*	Kubota (Mycogen Corp.)
Kareit MC	fenitrothion	Polyurethane	Sumitomo Chemical
Kayatack MC	chlorpyrifos	Polyurea	Nippon Kayaku
Lentrek 20MC	chlorpyrifos	melamine urea resin	Dow Elanco Nippon
Lumbert MC	fenitrothion	polyurethane	Sumitomo Chemical
Mocap 3MC	ethoprophos	melamine resin	Rhone-Poulenc Yuka Agro
Naramycin D80	cycloheximide	melamine resin	Tanabe Pharm,
Deet MC	DEET	melamine resin	SDS Biotech Toppan Moor
Sumi Cue-lure microcapsule sol	fenitrothion +Cue-lure	gelatin/gum arabic	Sankei Chemical, Toa Gosei
Sumipine MC	fenitrothion		Sumitomo Chemical
Sumithion MC	fenitrothion		Sumitomo Chemical
Sumithion MC for cockroach control	fenitrothion		Sumitomo Chemical

* These are trade names of each company.

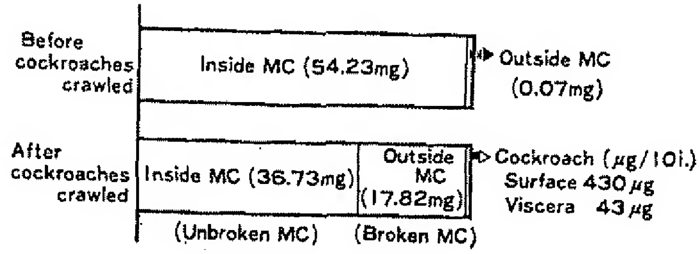

Figure 1. Distribution of fenitrothion (inside and outside the microcapsules) before and after cockroaches crawled on the microcapsule-treated petri dish. (From Tsuda, S., Ohtsubo, T., Kawada, H., Manabe, Y., Kishibuchi, H., Shinjo, G. and Tsuji, K., *J. Pesticide Sci.*, 12, 23, 1987. with permission.)

If the MC's are too weak, where D/T is large, initial efficacy is good but residual efficacy is poor. On the other hand, when the MC's are too strong and no breaking takes place, neither initial nor residual efficacy is good. When the cockroaches trample the MC's, the a.i. is released and kills the target insects. These MC's are activated only when the cockroaches make contact with them. This mechanism is similar to that of land mines. Therefore, these MC's could be called land mine-type MC's.

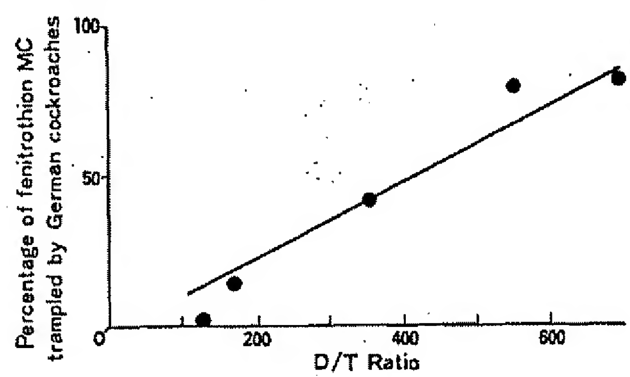

Figure 2. Relationship between the D/T ratio and the percentage of fenitrothion microcapsules (MC) trampled by German cockroaches on a petri dish after 2 hours. (From Ohtsubo, T., Tsuda, S., Kawada, H., Manabe, Y., Kishibuchi, N., Shinjo, G. and Tsuji, K., *J. Pesticide Sci.*, 12, 43, 1987. with permission.)

Discussion of physical strength of the MC's was also reported. The relationship between D/T and P_{50}, pressure at which 50% of the MC's were

broken, was explained by modifying the theory of destruction of an empty sphere with thin wall.[54]

A cyphenothrin microcapsule was also developed for cockroach control.[34] The mode of action is the destruction of MC's by cockroach trampling.

Diazinon was microencapsulated with a polyamide-polyurea wall.[9,60,67] This MC showed superior residual effect to EC against German cockroaches. The advantage of this product is reduction of toxicity and longer residual activity. This product is also active against diazinon-resistant cockroaches. This is due to the change of mode of action by microencapsulation. Diazinon is generally known to be active by contact poison. By the massive ingestion of MC's into the digestive tracts, which is specific for MC's, diazinon MC could be active against the diazinon-resistant cockroaches.

There are also reported fenitrothion and pyrethroid (fenvalerate and fenpropathrin) MC's for agricultural use whose mode of action is via breaking of MC.[50-52,83] For the fenvalerate MC against diamondback moth (*Platella xylostella*), it was found that there was a linear relationship between the LC_{50} and D/T ratio on a log-log graph paper.[50,83] Fenitrothion MC's showed similar biological behavior as that of fenvalerate MC.[50,83] These result indicate that D/T parameter, i.e., the strength of the MC, determines its efficacy. Thus, in these cases, the crushing of the MC's by the insects is the most important process in biological efficacy.

Fish toxicity against killifish (*Oryzias latipes*)[50,83,86] and mammalian toxicity LD_{50} (mg/kg)[51,76] of pyrethroid MC's were found to depend on DT, the parameter of the release rate of a.i. into water from MC's. Therefore fish toxicity and mammalian toxicity are controlled by diffusion of the a.i. into water.

Temperature-activated MC's have been developed by utilizing side chain crystallizable polymers (SCCP) with melting point in the 15-30°C range.[6,25,26,41] SCCPs have an acrylic backbone with a series of long chain fatty alcohols esterified to it as side chains. It is the ability of these chains to crystallize and then melt over a very narrow temperature range (5°C), that allows for differential temperature release rates of the a.i. The side chain length influences the release temperature of the polymer by changing the polymer melting point (Tm). Side chain lengths of 12-18 carbon units will give release temperatures of from 15 to 30 °C.

Diazinon MC's with Tm of 30°C were prepared.[6,26] The release rate of a.i. from MC's increased from 2.5μg/h at 20°C to 17μg/h at 32°C. The MC's gave significantly less control at 20°C, but control increased to 90% when the temperature increased to 32°C. The high level of control continued for 4-wk at 32°C. Thus, there was a higher level of control at temperatures higher than the polymer's glass transition temperature but less control below it.

Bacillus thuringiensis (Bt) was encapsulated in a starch matrix in order

to control the European corn borer.[13] Microencapsulation of pesticides in yeast was also reported.[31]

It is also expected that newer and simpler microencapsulation methods may be developed for preparing more functional microcapsules. An example is self-microencapsulation in which microcapsules are prepared merely by addition of a liquid formulation containing a wall forming monomer to water.[35,74] A sprayable, self-encapsulating starch formulation has also been developed.[65]

2. Polymeric Pesticides

Polymeric pesticides are obtained by bonding pesticides to polymers via covalent or ionic bonds to polymers. Polymeric pesticides are also obtained by binding pesticide first to monomers, followed by polymerization. Pesticide is released from the polymeric pesticide by hydrolysis or photolysis of the polymer-pesticide bond in the environment.[84]

A polymeric pesticide of chlordimeform for site-specific release control on cotton leaves was reported.[36] The following specific properties in the cotton leaf's microenvironment were to be utilized as a specific release trigger.

- pH values in the range of 8-10 existent on the leaf surfaces caused by alkaline excretions.
- the optimum orientation of the leaves to sunlight with its photochemical potency.
- cation concentration of 18-20 m moles/l found in cotton leaf dew.

Consequently, alkali-catalized hydrolysis, photolysis, and cation exchange have been identified as the most promising target-specific triggers to be utilized in the new site-specific release system for cotton. Preliminary greenhouse and field experiments have given evidence of the advantage of site-specific release systems. Especially light-triggered release as a concept showed the most promising results with respect to a remarkably prolonged duration of biological activity.

E. BIOPESTICIDE FORMULATIONS[1,2,22]

Biopesticides are based on naturally occurring toxins, and microorganisms such as fungi, bacteria, viruses, protozoa and nematodes are used in insect and weed control. Interest is growing in biological control agents because they are safe, nonpolluting, and sometimes more effective than chemical pesticides.

Microbial insecticides are extremely promising pest-control tools for use in IPM programs. Their mode of action is slower than conventional chemical insecticides. Microbiologicals are generally quite specific and therefore nontoxic to nontarget organisms, and they are less likely to cause insect resistance than are chemical insecticides.[2]

Biopesticides, however, have the problems of stability both during

storage and after application. Therefore, formulation research works are very important.

A particularly promising method to stabilize microbial insecticides is to encapsulate them in a pH-sensitive polymer that provides protection until the polymer is broken down by the high pH in the insect gut.[2,4]

After application, the microbial formulation is subject to various environmental degradation conditions such as leaf pH, leaf exudates and proteolytic enzymes, desiccation and sunlight. Microbial insecticides have been found to lose 50% of their activity within a few days by solar radiation. Optical brighteners have been found to give complete UV protection to viral insecticides.[66]

There are some other examples of microencapsulated biopesticides.[7,22,39,88] *Bacillus thuringiensis* (Bt) was microencapsulated in pre-gelatinized starch; the addition of congo red protected the Bt against UV degradation.[14,65] A sprayable self-encapsulating starch formulation was also developed. Pre-gelatinized starch, sucrose, and Bt were mixed in water, and sprayed to cotton leaves, and Bt was entrapped on the leaf surface after application. This MC had good rainfastness, and was effective against European corn borer (*Ostrinia nubilalis* Hübner) neonate larvae for more than 2 wk.[38]

Cellcap is a commercial product utilizing non-living bacterial cells of the genus *Pseudomonas fluorescense* as the walls for encapsulating the protein toxins from strains of *Bacillus thuringiensis*.[17,22,73] The bacteria are generally engineered to contain the Bt genes coding for the production of the toxins which accumulate within *Pseudomonas* cells during fermentation. The cells are then killed and stabilized, hardening the bacterial cell wall by crosslinking, and inactivation of biotoxin degrading enzymes within the cell. The process leaves the fully active biotoxin effectively encapsulated within the bacterial cell. This product showed good efficacy for diamondback moth on cabbage, partly due to the enhanced field persistence achieved by the stabilization process.[22]

Microencapsulation in living cells was also reported.[17,22] Bt toxin gene was integrated into the chromosome of *Pseudomonas fluorescense* by a gene replacement with the transposon Tn5.[49] The Tn5 transposon was made transposase minus by deleting the responsible region from the transposon and replacing it with the Bt endotoxin.

The living cell approach to biotoxin delivery has some potential advantages over non-living cells.[22] Since biotoxins such as the δ endotoxins of Bt must be ingested to be effective, it may be difficult to deliver them effectively in a non-living form to soil-bound roots. The living cells, however, can be applied to seeds prior to planting with the possibility that such cells may be able to colonize roots as the plant grows. A living cell could provide protection with only one application through a growing season.

It has been reported that biopesticides can be entrapped within a cross-linked matrix of organic polymers such as alginate, polyacrylamide, or carrageenan to form stable and uniform granules.[19] These formulations are relatively inexpensive and permit addition of nutrient bases, pesticides, or other compounds.

It is also reported that invert emulsions promote infection without a lengthy dew period, although fungi which attack weeds often require a lengthy dew period to effect infection.[5,56]

Pheromones and other attractants can be included to direct the pest to the insecticide.[90] This "attracticide" formulation can reduce amounts of insecticides.[3]

Combinations of herbicides and bacteria can significantly reduce herbicide use rate to control a broad spectrum of weed species.[8]

F. OTHER FUNCTIONAL FORMULATIONS

1. Jumbo Herbicides[32,48]

The Japan Association for Advancement of Phyto-Regulators (JAPR) has carried out basic research concerning large granular type herbicides, provisionally called Jumbo Pellet (JP), in an attempt to treat 0.3 ha paddy field within 5-6 min by throwing 20 JPs per 0.1 ha from levees into a paddy field. At present, "Jumbo" is a general term of the throw-in type herbicide formulations, and each formulation is about 50 g and applied 100-200 formulations per hectare from the levees by hand. Then they spread and diffuse easily in water. The advantages of Jumbo herbicides are as follows,

- Small and light: Dosage is 1/3 of usual application.
- Easy application and labor saving: They can be applied by hand from levees.
- Dust free and no drift: Safe for both workers and adjacent plants.
- Proper application: Depending on the area of the field, appropriate numbers of the formulations are thrown at equal distance.
- Reduced cost of rice crop: Costs of delivery and storage of the formulation becomes cheaper.
- Applicable even in bad conditions: They can be applied even on windy days.

Jumbo herbicides are classified into two types. One is on effervescent tablet type. The other is water soluble package type. Effervescent tablets are formulated by using solid acid, carbonate, and dispersants. When these tablets are put into water, they effervesce vigorously and spread over a broad area. Active ingredients spread smoothly in the paddy field and become uniform within 6-24 hr. Water-soluble bags of herbicide granules are also available.

2. Water Surface Spreading Formulations

Water surface spreading granules of cycloprothrin are formulated by

using potassium chloride as a carrier in order to control rice water weevil.[63] This formulation is made mostly by impregnation of active ingredient solution into granulated carriers. After application to the paddy field, granules sink temporarily down onto the soil. Then potassium chloride dissolves and granules resurface and float. Finally, the active ingredient solution spreads in all directions on the water surface. Rice water weevils, *Lissorhoptrus oryzophilus* live in paddy water and on rice plants, and touch the water surface. Therefore, this formulation can deliver the high concentration of the active ingredient to the place where target rice water weevils are living to result in good control. For this reason, this granule could be said to be a site-specific formulation.

Binders in the granules are very important to resurface the granules. The binders act as a trap of air in the granules after dissolution of potassium chloride in water that result in resurfacing of the granules. Therefore the binders should not dissolve completely but remain viscous and keep their binding property for some time. For such binders, a combination of high molecular weight sodium polyacrylate and xanthan gum is the best.

In order to spread the active ingredient on the water surface, organic solvents and surface active agents are used. In this case, the diisodecylphthalate is used as a solvent and use of the block copolymers of ethyleneoxide and propyleneoxide as the surfactants is appropriate.

These granules are also packaged in water-soluble bags,[37] and are applied by throwing ten, 60-g bags from levees by hand. The advantages obtained are similar to those from jumbo herbicides. When these water-soluble bags are applied to water they dissolve within a few minutes. The granules resurface for about 4 hours and the oily active ingredients spread on the water surface to control rice water weevil.

It has recently been shown that the technology using potassium chloride as the carrier allows the herbicides to spread and diffuse sufficiently over the paddy field. In this instance, a water-soluble bag is seen as being applicable for the packaging of such jumbo herbicides.

Floating carriers such as foaming perlite and silicone surfactants are also applied to help the granules float, spread and diffuse on the water surface after application in water soluble bags.[47]

A water-surface-spreading oil formulation has also been developed.[15] This formulation is put drop by drop into the paddy field from bottles, which are hung from poles. Oily active ingredients immediately spread on the water surface. The oily film adheres to leaf sheaths and leaves of the rice plant. Surface tension and capillary action assure control of the rice insects even with changes in either the water level from rain or growth of rice plant, and control insect pests of rice crop. This application method is effective even in rainy condition and it provides for substantial reductions in labor requirements.

3. 1 kg Granule[72,76-79,85]

In Japan, herbicide granules are packed in 3-kg packages that will treat 0.1 hectares. Recently, however, JAPR proposed to reduce the dosage to 1-kg /0.1-ha (1-kg granule). The 1-kg granule was developed to save application labor in paddy field and also to reduce distribution and storage charges. The 1-kg granules contain 3 times the amount of active ingredients as compared to the 3-kg granules. The 1-kg granules are designed to be spread from the levees of the paddy field which has a 30-m total width. Therefore, the particle diameter needs to be 1.0-1.5 mm (mainly 1.2mm) to reach out 15 m from each levees by the power spreader (the particle diameter of the 3-kg granules is 0.8- 0.9mm). Thus, there are about 400 granules in 1g of 1-kg granule as compared to ca. 1000 granules in 1g of 3-kg granules. This results in about 4 granules of 1-kg granules/100 cm^2 while there is 30 granules of the 3-kg material/100 cm^2. Thus the number of granules of 1 kg granules per unit area is about one eighth of that of 3 kg granules. In order to get stable herbicidal efficacy, it is essential to maximize the diffusion of the active ingredients in paddy water by either making smaller particle sizes of the active ingredients, and/or selecting of appropriate surfactants. With recent improvements, the 1-kg granules now give sufficient herbicidal efficacy.

V. CONCLUSIONS AND FUTURE TRENDS

Recent trends are moving toward developing safer pesticides, more efficient and more labor-saving formulations, and new application technologies. Therefore development of highly effective, but short-lived and biorational active ingredients at reduced dosage is essential. For this purpose, research work for pesticide delivery systems becomes important. By advance of formulation technologies, various new functional formulations have been developed along this line, which achieve targeting, improve safety for workers and environment, reduce toxicity, increase biological efficacy, and save labor in the field. For example, there have been developed the microcapsules for cockroach control, whose mode of action is trampling of the microcapsules by cockroaches, water surface spreading formulations as site-specific ones, temperature-activated microcapsules and polymeric pesticides which are activated by water, UV light, or ions. For targeting, spray nozzles with the sensors that detect the targets have also been developed. The trend is to develop more various stimuli-responsive formulations and application technologies.

Biopesticides are safe, nonpolluting, and target specific. Therefore they are very promising and will be used more widely, but their formulations must be stabilized by various methods.

The probability of discovering new pesticides through screening has decreased. It has become very difficult to develop new pesticides, and cost

and time for development of the new pesticides has increased significantly. Therefore, the development of new functional formulations and new application fields for existing pesticides is comparable to the invention of new pesticides. Thus, the cost and time required for such development would be less than that needed for the development of new pesticides. For example, fenitrothion microcapsules for termite control were recently developed. Fenitrothion is effective against termites but it decomposes on soil. Therefore, conventional formulations of fenitrothion could not be used for termite control. Microencapsulation protects fenitrothion from contact with soil and reduces decomposition. By this method, a new formulation and a new application field for fenitrothion were developed.

For labor saving, various formulations and applications methods have been developed. In these cases, formulations have been developed to integrate into their containers and application methods. There are examples where the containers themselves function as the applicators, e.g. pesticide applications from the levees and irrigation inlets in paddy fields.

In order to improve safety for workers and reduce the container disposal problem, water-soluble packages have been developed. This technology will be more widely used in future agricultural formulations. Closed transfer systems and returnable and mini-bulk containers are also used in the United States.

In the future, it is considerably desired to develop intelligent pesticide formulations and application technologies, which have sensing, processing, and activating functions. Then pesticide application will become very efficient, safe, and labor saving. Further development of these new functional formulations and application technologies are highly expected.

ACKNOWLEDGMENTS

I wish to thank Agros Corporation for permission to publish this work. I also thank Mr. H. Kobayashi for preparation of the manuscript.

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